

REMARKS/ARGUMENTS

Claims 1-4 are pending. Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Rejection under 35 USC 102(e)

Claims 1 and 4 stand rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Vidyadhar et al. US 6,649,765. This rejection is respectfully traversed.

In Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (MPEP 2131), the CAFC set forth that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference". In the instant case, not every element of the claims is present in the '765 Vidyadhar patent.

Here, the Examiner argues that donepezil hydrochloride was dissolved in residue of free base concentrated from methylene dichloride solvent system adding a methanol and methanolic HCl mixture, then the solvents were removed to obtain a "solid" (citing '765 at col. 4, example 2), and concludes that anticipates the claims. The Examiner further alleges that a solid being silent about its crystallinity is noncrystalline or amorphous.

However, the claims are drawn to a process for preparing donepezil hydrochloride wherein donepezil hydrochloride is dissolved in a mixture of an alcohol and a chlorinated solvent and then the solvents are removed from the solution. This is in contrast to the disclosure of the '765 Vidyadhar patent. Example 2 of the '765 Vidyadhar patent discloses preparing donepezil free base in methylene chloride, then removing the methylene chloride. In an additional step, the

Application No. 10/509,952
Amendment Dated 11/9/2007
Reply to Office Action of August 10, 2007

donepezil free base is dissolved in methanol, followed by addition of hydrochloric acid. So, there is not a disclosure in the '765 Vidyadhar patent of donepezil hydrochloride dissolved in a mixture of an alcohol and a chlorinated solvent.

The Examiner argues that a solid being silent about its crystallinity is noncrystalline or amorphous, but cites no art to stand for this proposition. If the Examiner is arguing that the '765 Vidyadhar patent inherently discloses the amorphous form of donepezil hydrochloride as instantly claimed, then the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. In re Rijckaert, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Here, the Examiner has not met that burden by arguing that Applicant needs to show the absence of an alleged effect. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

Accordingly, reconsideration and withdrawal of the rejection of claims 1 and 4 under 35 USC 102(b) is respectfully requested.

Application No. 10/509,952
Amendment Dated 11/9/2007
Reply to Office Action of August 10, 2007

Rejection under 35 USC 103(a)

Claims 1-4 stand rejected under 35 U.S.C. 1 03 (a) as allegedly being unpatentable over Vidyadhar et al US 6,649,765 in view of Imai et al US 5,985,864. This rejection is respectfully traversed.

The Examiner argues that the '765 Vidyadhar patent disclosed an anticipatory process and that the broader scope of claims 1 and 4 encompass mixture of solvents beyond the residue amount or a different choice of combination, or that the method of solvent removal being particularly vacuum drying or spray drying are prima facie obvious variation of the Vidyadhar et al. '765 process. The Examiner further argues that it is conventionally known that donepezil hydrochloride are soluble in a variety of solvents (citing Imai et al. '864, entire document), and vacuum or spray drying are conventional laboratory choices of solvent removing procedure.

However, the claims are patentable over the combination of the '765 Vidyadhar and '864 Imai patents for the following reasons. To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488 (Fed. Cir. 1991). MPEP 2143. To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the

Application No. 10/509,952
Amendment Dated 11/9/2007
Reply to Office Action of August 10, 2007

prior art. In re Royka, 490 F.2d 981 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." In re Wilson, 424 F.2d 1382, 1385 (CCPA 1970). MPEP 2143.03. It is important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. (JKS v Teleflex, 12 S.Ct. 1727, 1740 (US 2007)). Often, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. (*Id.*).

Here, not every element of the claims is taught or suggested in the combination of the '765 Vidyadhar and '864 Imai patents. As set forth above, the claims are drawn to a process for preparing donepezil hydrochloride wherein donepezil hydrochloride is dissolved in a mixture of an alcohol and a chlorinated solvent and then the solvents are removed from the solution. This is in contrast to the disclosure of the '765 Vidyadhar patent. Example 2 of the '765 Vidyadhar patent discloses preparing donepezil free base in methylene chloride, then removing the methylene chloride. In an additional step, the donepezil free base is dissolved in methanol, followed by addition of hydrochloric acid. So, there is not a disclosure in the '765 Vidyadhar patent of donepezil hydrochloride dissolved in a mixture of an alcohol and a chlorinated solvent. This deficiency is not addressed by the '864 Imai patent.

While the '864 Imai patent discloses several polymorphs of donepezil hydrochloride, it

Application No. 10/509,952
Amendment Dated 11/9/2007
Reply to Office Action of August 10, 2007

does not teach or suggest amorphous donepezil hydrochloride prepared by dissolving donepezil hydrochloride in a mixture of an alcohol and a chlorinated solvent. The '864 Imai patent does not teach or suggest a chlorinated solvent is selected from the group consisting of chloroform, methylene dichloride, carbontetrachloride and ethylene dichloride.

The Examiner argues the motivation is provided in that one having ordinary skill in the art in possession of general laboratory skill and the Imai et al '864 reference would be in possession of the instant claims because a proven process was disclosed by Vidyadhar '765, the optional choices of solvents wherein donepezil hydrochloride is soluble have been provided by Imai, and that therefore, one having ordinary skill would pick and choose any of the solvent or mixture of solvents wherein donepezil hydrochloride is soluble for the process and employ anyone of the solvent removing technique for solvent reduction depending on resource availability. The Examiner further argues that picking and choosing an effect oriented condition in a chemical process is *prima facie* obvious in the chemical art, especially, such picking and choosing has been conventionally evidenced to be operable. In re Szumski 133 USPQ 551. However, as set forth above, the '765 Vidyadhar patent does not teach or suggest donepezil hydrochloride dissolved in a mixture of an alcohol and a chlorinated solvent, and this is also not taught or suggested in the '864 Imai patent. Since the combination of the patents does not disclose or suggest these limitations, there is no motivation to combine the references to reach these limitations, and no expectation of success.

Accordingly, reconsideration and withdrawal of the rejection of claims 1-4 under 35 USC 103(a) is respectfully requested.

Application No. 10/509,952
Amendment Dated 11/9/2007
Reply to Office Action of August 10, 2007

Claims 1-4 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Sugimoto et al. US 4,895,841 or Vidyadhar et al. US 6,649,765, or Imai et al. US 5,985,864 in view of Lieberman et al. and Brittain. This rejection is respectfully traversed.

The Examiner argues that Sugimoto et al. (col. 34 example 4) or Vidyadhar et al. '765 (col. 4, example 2) disclose a process of making donepezil hydrochloride of the claims. The Examiner further argues that Imai et al. '864 disclosed multiple variations of modifying the process of making donepezil hydrochloride to obtain variations of crystalline and pure forms of the compound. The Examiner admits that the difference between the prior art processes and the instantly claimed process is that the products being made are crystalline or solids, and using mixtures of more limited solvent combinations, and/or the method of solvent removal being particularly vacuum drying or spray drying. However, the Examiner alleges that it is conventionally known that donepezil hydrochloride is soluble in a variety of solvents (citing Imai et al. '864 entire document), and further alleges that it is a conventional teaching that amorphous is more desirable than crystalline form when formulation into pharmaceutical compositions (citing Lieberman p.463 last paragraph) and the conventional process for obtaining amorphous material are spray drying or vacuum drying i.e. lyophilization (citing Brittain).

Here, not every element of the claims is taught or suggested in the combination of the '765 Vidyadhar and '864 Imai patents. As set forth above, the claims are drawn to a process for preparing donepezil hydrochloride wherein donepezil hydrochloride is dissolved in a mixture of an alcohol and a chlorinated solvent and then the solvents are removed from the solution. This is in contrast to the disclosure of the '765 Vidyadhar patent. Example 2 of the '765 Vidyadhar

patent discloses preparing donepezil free base in methylene chloride, then removing the methylene chloride. In an additional step, the donepezil free base is dissolved in methanol, followed by addition of hydrochloric acid. Accordingly, there is not a teaching or suggestion in the '765 Vidyadhar patent of donepezil hydrochloride dissolved in a mixture of an alcohol and a chlorinated solvent. In addition, there is not a teaching or suggestion in the '841 Sugimoto patent of donepezil hydrochloride dissolved in a mixture of an alcohol and a chlorinated solvent. Example 4 of the '841 Sugimoto patent as cited by the Examiner discloses donepezil base dissolved in methylene chloride, to which a 10% solution of hydrochloric acid in ethyl acetate is added, followed by concentration in vacuo to obtain a crystal, which was recrystallized from methanol/Isopropyl ether. This deficiency is not addressed by the '864 Imai patent. While the '864 Imai patent discloses several polymorphs of donepezil hydrochloride, it does not teach or suggest amorphous donepezil hydrochloride prepared by dissolving donepezil hydrochloride in a mixture of an alcohol and a chlorinated solvent. The '864 Imai patent does not teach or suggest a chlorinated solvent is chloroform, methylene dichloride, carbontetrachloride or ethylene dichloride.

In addition, there is no motivation for one of skill in the art to alter the methods of the '841 Sugimoto patent, the '765 Vidyadhar patent, or the '864 Imai patent to arrive at the claimed method, and no reasonable expectation of success. There is no teaching or suggestion within the Lieberman and Brittain references to alter the method as taught by the '841 Sugimoto patent, the '765 Vidyadhar patent, or the '864 Imai patent to arrive at the instantly claimed method.

The Examiner argues the motivation is provided in that one having ordinary skill in the

Application No. 10/509,952
Amendment Dated 11/9/2007
Reply to Office Action of August 10, 2007

art in possession of the purified crystalline or solid material of the compound donepezil hydrochloride would be motivated to prepare an amorphous form of the product because it is conventional state of the art that "[t]heoretical considerations predict that amorphous solids will in general, be better absorbed than will crystalline ones" (see Lieberman p. 463) and the procedure for obtaining amorphous forms have been conventionally well delineated using a spray drying or vacuum drying process (Brittain). The Examiner further argues that the claims would have been obvious because an ordinary skilled person "has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." KSR 82 USPQ2d 1385, 1390. However, in the KSR case, the Court noted that the analysis supporting a rejection under 35 USC 103(a) should be made explicit, and that it was "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does". KSR, slip op. at 15. The Court further stated that:

Often, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit. See *In re Kahn*, 441 F. 3d 977, 988 (CA Fed. 2006) ("[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness"). KSR, slip op. at 14.

In a Memorandum dated May 3, 2007, Margaret A. Focarino pointed out that that:

Therefore in formulating a rejection under 35 U.S.C. § 103(8) based upon a combination of prior art elements, it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed.

Here, there is not a combination of prior art elements, since no reference, or combination of references, teaches or suggests a process for preparing donepezil hydrochloride wherein donepezil hydrochloride is dissolved in a mixture of an alcohol and a chlorinated solvent and then the solvents are removed from the solution. In addition, Applicant has shown that there is not a reason why a person of ordinary skill in the art would be motivated to practice a process for preparing donepezil hydrochloride wherein donepezil hydrochloride is dissolved in a mixture of an alcohol and a chlorinated solvent and then the solvents are removed from the solution. Accordingly, reconsideration and withdrawal of the rejection of pending claims 1-4 is respectfully requested.

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Application No. 10/509,952
Amendment Dated 11/9/2007
Reply to Office Action of August 10, 2007

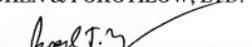
For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

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